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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STOCKTON, LAURA LYNNE	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,135	OKU ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,4,6 and 11-14* is/are allowed.

6)☒ Claim(s) *2,3,5,8 and 10* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 and 10-14 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 21, 2004 has been entered.

The indicated allowability of claims 7 and 8 is withdrawn in view of the objection and rejection below.

Rejections made in the previous Office Action which do not appear below have been overcome by Applicants amendment to the claims. Therefore, arguments pertaining to these rejections will not be addressed.

Claim Objections

Claim 7 is objected to since the claim does not state that the compound of claim 1 is in admixture with a pharmaceutically acceptable organic or inorganic excipient (see page 21, lines 5-9).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case, Applicants are claiming a pharmaceutical preparation (claim 8) for the prophylaxis or treatment of a number of diseases (e.g., diabetes, diabetic complications, polycystic ovary syndrome, skin disorders, etc.). Applicants also are claiming (claim 10) a method of preventing or treating a number of the same diseases.

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The various diseases/disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. For example, Applicants claims embrace a method of preventing or treating diabetic complications. The instant specification does not give any guidance as to the full range of diabetic complicating

diseases that could be treated or prevented using the instant claimed process. In order to practice the claimed invention, one skilled in the art would have to speculate which diabetic complicating diseases/disorders could be treated or prevented using the compounds found in the instant claims. The number of possible diabetic complicating diseases/disorders embraced by the claims would impose undue experimentation on the skilled art worker. Applicants have not demonstrated that all of the diseases/disorders embraced by instant claims 8 and 10 could be prevented or treated. Therefore, based on the unpredictable nature of the invention, and the state of the prior art would prevent one skilled in the art from accepting any therapeutic regimen on its face.

Response to Arguments

Applicants' arguments filed March 18, 2004 have been fully considered. Applicants argue that the subject compounds have

hypoglycemic activity and medical procedures for treatment of patients with hypoglycemically active pharmaceutical compounds are well known.

In response, and as argued by Applicants, treatment of patients with certain diseases/disorders with hypoglycemically active compounds is known. However, prevention or treatment of the multitude of diseases/disorders which are found in the instant claims using the same compound is not. The various diseases/disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. Therefore, the claims as such lack enablement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3, and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention.

Claim 2 does not further limit claim 1 {see definition (10) under variable R^6}. Compounds 30 and 31 in claim 5 are not embraced by claim 1 (see the R^1 definition and the possible substituents).

Response to Arguments

Applicants' arguments filed March 18, 2004 have been fully considered. In regard to the rejections of claims 2 and 5 under 35 USC 112, second paragraph, Applicants argue that R^1 in claim 1 is defined as "an aryl which is substituted by halogen at the ortho position relative to the point of attachment of R^1 to A". Applicants argue that claim 1 further states that "aryl" is defined as unsubstituted aryl or alkyl-substituted aryl. Applicants further argue that substitution of an aryl radical can be on a side chain.

In response, Applicants' arguments have been considered. Applicants submitted literature has also been considered. However, Applicants' arguments have not been found persuasive. Claims 2 and 5 fail to further limit claim 1.

The definitions of "alkyl" (page 4, lines 9-27), "aryl" (page 6, lines 34-38) and "alkyl-substituted aryl" (page 6, lines 39-40 and page 7, lines 1-6) have again been reviewed. See following each of these definitions that have been reproduced from the instant specification.

"Alkyl" and "alkyl moiety" are each preferably linear or branched alkyl. Preferable specific examples include methyl, ethyl, 1-propyl, i-propyl, 1-butyl, i-butyl, t-butyl, sec-butyl, 1-pentyl, i-pentyl, sec-pentyl, t-pentyl, methylbutyl, 1,1-dimethylpropyl, 1-hexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1-ethylbutyl, 2-ethylbutyl, 3-ethylbutyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1-ethyl-1-methylpropyl, 1-heptyl, 1-methylhexyl, 2-methylhexyl, 3-methylhexyl, 4-methylhexyl, 5-methylhexyl, 1-ethylpentyl, 2-ethylpentyl, 3-ethylpentyl, 4-ethylpentyl, 1,1-dimethylpentyl, 2,2-dimethylpentyl, 3,3-dimethylpentyl, 4,4-dimethylpentyl, 1-propylbutyl, 1-octyl, 1-methylheptyl, 2-methylheptyl, 3-methylheptyl, 4-methylheptyl, 5-methylheptyl, 6-methylheptyl, 1-ethylhexyl, 2-ethylhexyl, 3-ethylhexyl, 4-ethylhexyl, 5-ethylhexyl, 1,1-dimethylhexyl, 2,2-dimethylhexyl, 3,3-dimethylhexyl, 4,4-dimethylhexyl, 5,5-dimethylhexyl, 1-propylpentyl, 2-propylpentyl and the like.

Of these, particularly preferred is alkyl having 1 to 6 carbon atoms.

In the present specification, "aryl" and "aryl moiety" are each unsubstituted aryl or alkyl-substituted aryl. Examples of preferable unsubstituted aryl include C_6 - C_{10} aryl, such as phenyl, naphthyl and pentalenyl. Of these, preferred are phenyl and naphthyl.

"Alkyl-substituted aryl" means aryl substituted by at least one alkyl. The number of alkyl substituents is preferably 1 to 4.

> The aryl moiety of "alkyl-substituted aryl" is the same as for the aforementioned unsubstituted aryl, and the "alkyl moiety" is as defined above, which is preferably lower alkyl. Specific examples of preferable alkyl-substituted aryl include tolyl, xylyl, mesityl, ethylphenyl, propylphenyl and the like, with more preference given to p-tolyl.

The specification discloses that the alkyl can be linear or branched. The definition of alkyl does not state that the "alkyl" can be substituted. An example given for an "alkyl-substituted aryl" is a group such as *p*-tolyl (e.g., a phenyl ring substituted with an methyl group at the *para*-position of the phenyl ring). Nothing in the original filed claims or the instant specification would lead, suggest, or teach to one skilled in the art to substitute any of the claimed substituents of definitions (1)-(11), under R^1 in claim 1, on the "alkyl" portion of the "alkylaryl" (which is embraced by the definition of "aryl") instead of the aryl portion of the "alkylaryl". It is also noted that in every other instance in the claims, Applicants were very specific about which substituents were optionally substituted with specific substituents {e.g., Claim 1, under the R^1 definition, definition (4), (7), etc.}.

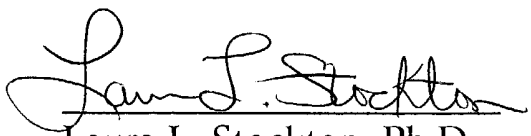
Allowable Subject Matter

Claims 1, 4, 6, 7 and 11-14 are allowed over the art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.



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April 28, 2004